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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Sangita Phadtare

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EXAMINER

KERR, KATHLEEN M

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 11/06/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/805,681

Applicant(s)

PHADTARE ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 1-6 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 6, mailed on July 22, 2002), Applicants filed an election received on August 14, 2002 (Paper No. 7). Claims 1-14 are pending in the instant Office action.

Election

2. Applicant's election without traverse of Group II, Claims 7-13, in Paper No. 7 is acknowledged. Claims 1-6 and 14 are withdrawn from further consideration as non-elected inventions. Claims 7-13 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/228,727 filed on August 29, 2000 as requested in the declaration and the first lines of the specification. The Examiner notes that the protein sequence of the claimed DHCP efflux protein is disclosed in said provisional application, but not the encoding DNA sequence itself as being examined herein.

Information Disclosure Statement

4. The information disclosure statement filed on April 15, 2002 (Paper No. 5) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy. The Examiner notes the incomplete citation of Phadtare *et al.* The Examiner has completed the reference and considered the entire document; no further action is required by Applicants.

Declaration

5. The declaration submitted by Applicants at the time of filing is sufficient in the instant application. The Examiner notes, however, that the declaration cites a different title from that noted on the first page of the application papers and the order of inventors are different. Both the title and order of listed inventors have been taken from the first page of the specification. Applicants should file a petition to correct the filing receipt *only* if this is unacceptable.

Drawings

6. The drawings have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Compliance with the Sequence Rules

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

- a) In Figure 4, 10 amino acid sequences are described without SEQ ID NOs.
- b) In Figure 6, 1 DNA sequence is described without a SEQ ID NO.
- c) In Figure 7, 1 DNA sequence is described without a SEQ ID NO.

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If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Objections to the Specification

8. The specification is objected to for being confusing concerning inclusion of sequences in the sequence listing. The Examiner notes that no SEQ ID NOs are mentioned in the specification or the claims. All sequences in the sequence listing must be described in the specification to clearly identify their input into the sequence listing. Correcting the above errors in the Figures 6 and 7 will apparently obviate this objection.

9. The Examiner notes that the pagination of the instant application was unclear in the absence of page numbers as originally filed. In a telephone interview with Applicants' representatives on October 23, 2002, appropriate pagination was discussed. The Examiner has added page numbers to the instant specification appropriately per that conversation.

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10. The specification is objected to because the Abstract does not completely describe the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name the source species, *Escherichia coli*, for completeness.

11. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Gene encoding a 4,5-dihydroxy-2-cyclopenten-1-one (DHCP) efflux protein promoting resistance to DHCP---

Claim Objections

12. Claims 9, 11, and 13 are objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The instant claims attempt to limit the subject matter of their respective parent claims using an inherent property described in the specification (see page 7, for example). However, this inherent property is the basis of the definition of the *dep* gene, as claimed in the parent claims. Thus, the function is also inherent in the parent claims and cannot be added to further limit their subject matter.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 7-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviation “DHCP” must be defined upon its first appearance in the claims for clarity. In Claim 1, the Examiner suggests changing “DHCP” to ---4,5-dihydroxy-2-cyclopenten-1-one (DHCP)---.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 7-13 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 7 is drawn to a gene that is claimed solely by the function of the encoded protein and without any structural limitations. The limitation of originating from *E. coli* in Claim 8 adds no structural limitation.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’

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of the claimed subject matter sufficient to distinguish it from other materials.” *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a gene encoding a DHCP efflux protein, a likely transmembrane protein specific for DHCP with respect to some other, common, structurally-distinct antibiotics, is briefly described having been obtained from *E. coli*. Only a single member of the genus is described. In the claims, this gene is only described according to the functional characteristics of the enzyme it encodes; no structural relationship is described or used in the claims. The limitation of the *E. coli* gene reduces the size of the claimed genus; however, only a single member of this smaller genus is described with no indication of structural similarities among the members of the genus. Thus, one of skill in the art would be unable to predict the structure of other members of this genus (either the broader genus of Claim 7 or the smaller genus of Claim 8) by virtue of the instant disclosure. Therefore, claims drawn to genes, plasmids, and bacteria containing the genus of said genes are not adequately described.

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The Examiner suggests the addition of structural language, such as being related to SEQ ID NO:1 or encoding the protein sequence (not yet in the sequence listing but depicted in Figure 4) to obviate the instant rejection.

15. Claims 7 and 9-13 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for the *dep* gene from *E. coli*, does not reasonably provide enablement for any *dep* gene, plasmid or host cell thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To make all members of the claimed genus would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the

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presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification presents no guidance or working examples for the production of a *dep* gene other than that which is described in SEQ ID NO:1. No description of other possible sources, in which a *dep* gene might be found, is mentioned in the specification or the art. Very little is known about the antibacterial DHCP and about any possible transmembrane proteins that can serve as efflux pumps to promote resistance to DHCP. This lack of information in the art is likely due to the uncommon nature of this particular antibiotic. While the skill in the art is high considering hybridization screening techniques, the predictability is low considering the entire lack of information about other DHCP efflux proteins and their presence in other bacteria. Thus, the instant claims are not enabled to the full extent of their scope.

The Examiner suggests the addition of structural language, such as being related to SEQ ID NO:1 or encoding the protein sequence (not yet in the sequence listing but depicted in Figure 4) to obviate the instant rejection.

Claim Rejections - 35 U.S.C. §§ 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

16. Claims 7-9 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The requisite “invention” or “discovery” in 35

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U.S.C. § 101 for a composition of matter requires the isolation of any naturally-occurring composition of matter; this is the idea of the input of “hand-of-man” into the invention or discovery. The Examiner suggests inserting the term “isolated” before the claimed product in the preamble.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 7-9 are rejected under 35 U.S.C. § 102(b) as being anticipated by Blattner *et al.* (The Complete Genome Sequence of *Escherichia coli* K-12. Science (1997) 277:1453-1474) and GenBank Accession Number AE000261. The instant claims are drawn to the *E. coli dep* gene identified in the specification as SEQ ID NO:2, which contains the coding sequence for the efflux protein conferring DHCP resistance.

Blattner *et al.* teach a stretch of DNA from the *E. coli* genome encoding a putative transport protein from 4627 bp to 5838 bp named *ydhC* (see GenBank Accession Number AE000261 for numbering). This DNA is identical to SEQ ID NO:2 (see attached alignment). This DNA also has the inherent property of encoding a protein conferring DHCP resistance when present in multiple copies.

The Examiner notes that on page 10 of the instant specification, the GenBank reference noted above is admitted as prior art.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

18. Claims 10-13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Blattner *et al.* (see above) and GenBank Accession Number AE000261 in view of Weickert *et al.* (Optimization of heterologous protein production in *Escherichia coli*. Current Opinion in Biotechnology (1996) 7:494-499). The instant claims are drawn to multicopy plasmids containing the *dep* gene from *E. coli* and bacteria cells containing said plasmids.

Blattner *et al.* teach as described above. Blattner *et al.* do not teach the disclosed gene in a multicopy plasmid in host cells.

Weickert *et al.* teach the heterologous expression of proteins in *E. coli* using multicopy plasmids to achieve good protein production (see Table 1, page 495).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Blattner *et al.* and Weickert *et al.* to make multicopy plasmids for expression in bacterial host cells because Blattner *et al.* specifically suggest “analysis of biochemical and catalytic properties of the expressed proteins” (see page 1461, left column) and Weickert *et al.* specifically teach multicopy plasmids as a technique for optimizing heterologous protein overproduction, which overproduction is required for protein purification and activity assays. One would have been motivated to combine the above

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teachings to overproduce the encoded protein, which Blattner *et al.* describe as a putative transport membrane protein *ydhC*, to attribute a specific function to the protein – a common practice in the art.

Conclusion

19. Claims 7-13 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK

November 4, 2002

